IN THE SPECIFICATION

Please amend the specification as indicated:

On page 8, lines 3-15

A second consideration of importance when using the compositions and methods of the present invention is the use and nature of penetration enhancers and carriers. Penetration enhancers facilitate the transport of drug molecules ~~molecues~~, for example, oligonucleotides and other nucleic acids, across mucosal and other epithelial cell membranes. Penetration enhancers include, but are not limited to, members of molecular classes such as surfactants, fatty acids, bile salts, chelating agents, and non-chelating non-surfactant molecules. Carriers are inert molecules that may be included in the compositions of the present invention to interfere with processes that lead to reduction in the levels of bioavailable nucleic acid or oligonucleotide drug.

On page 13, lines 6-32

Transdermal drug delivery is a valuable route for the administration of lipid soluble therapeutics. It has been recognized that the dermis is more permeable than the epidermis and therefore ~~therfore~~ absorption of drugs is much more rapid through abraded, burned or denuded skin. Inflammation and other physiologic conditions that increase blood flow to the skin also enhance absorption via the transdermal route. Absorption by this route may be enhanced via the use of an oily vehicle (inunction) or through the use of penetration enhancers. Hydration of the skin and the use of controlled release topical patches are also effective ways to administer drugs via the transdermal route. This route provides a means to deliver the drug for both systemic and local therapy.

Ocular delivery of drugs is especially useful for the local treatment of eye infections or abnormalities. The drug is typically administered via instillation and absorption of the drug occurs through the cornea. Corneal infection or trauma may thus result in more rapid absorption. Ophthalmic ~~Opthalmic~~ delivery systems that provide prolonged duration of action (e.g., suspensions and ointments) and ocular inserts that provide continuous delivery of low amounts of drugs are useful additions to ophthalmic therapy. The ocular delivery of drugs results in predominantly local effects. Systemic

absorption that results ~~reults~~ from drainage via the nasolachrimal canal is limited and few systemic side effects are typically observed.

On page 36, line 28 to page 37, line 2

Antisense compounds may alternatively or additionally comprise a synthetic moiety having nuclease activity covalently linked to an oligonucleotide having an antisense sequence instead of relying upon recruitment of an endogenous nuclease. Synthetic moieties having nuclease activity include, but are not limited to, enzymatic RNAs (as in ribozymes), lanthanide ion complexes ~~comlexes~~, and the like (Haseloff *et al.*, *Nature*, 1988, *334*, 585; Baker *et al.*, *J. Am. Chem. Soc.*, 1997, *119*, 8749).

On page 91, line 30 to page 92 line 2

Formulation 12a: A solution of ISIS 2302 was prepared by mixing 5 ml ISIS 2302 stock solution(100 mg/mL) with 95 ml sterile saline to have a final concentration ~~cincentration~~ of 5 mg/ml.